

PATENT COOPERATION TREATY

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From the
INTERNATIONAL SEARCHING AUTHORITY

To: <div style="position: absolute; top: 150px; left: 200px;">see form PCT/ISA/220</div> <div style="position: absolute; top: 100px; right: 100px; text-align: right;"> PCT REC'D 24 JUL 2006 WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1) </div> <div style="position: absolute; top: 140px; left: 400px; transform: rotate(-15deg);">PT02</div>		Date of mailing (day/month/year) see form PCT/ISA/210 (second sheet)
Applicant's or agent's file reference see form PCT/ISA/220		FOR FURTHER ACTION See paragraph 2 below
International application No. PCT/GB2005/004990	International filing date (day/month/year) 21.12.2005	Priority date (day/month/year) 21.12.2004
International Patent Classification (IPC) or both national classification and IPC INV. C07C39/15 C07C235/26 C07C233/03 C07D213/02 A61K31/055 A61K31/05 A61K31/167 A61K31/165 A61P21/00		
Applicant UCL BIOMEDICA PLC		

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 68.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA: <div style="display: flex; align-items: center;"> <div> European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465 </div> </div>	Date of completion of this opinion see form PCT/ISA/210	Authorized Officer Grammenoudi, S Telephone No. +49 89 2399-8324
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WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/GB2005/004990

Box No. I Basis of the opinion

1. With regard to the language, this opinion has been established on the basis of:
 - ☒ the international application in the language in which it was filed
 - ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ on paper
 - ☐ in electronic form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in electronic form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/GB2005/004990

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of

☐ the entire international application

☒ claims Nos. 34-39

because:

☒ the said international application, or the said claims Nos. 34-39 relate to the following subject matter which does not require an international search (*specify*):

see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed (*specify*):

☐ no international search report has been established for the whole application or for said claims Nos.

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13ter.1(a) or (b).

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-bis of the Administrative Instructions, and such tables were not available to the International Searching Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☐ See Supplemental Box for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2005/004990

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	6,7,10,12,17,43-45
	No: Claims	1-5,8,9,11,13-16,18-42
Inventive step (IS)	Yes: Claims	
	No: Claims	1-45
Industrial applicability (IA)	Yes: Claims	1-33,40-45
	No: Claims	34-39

2. Citations and explanations

see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

- D1= WO-A-04/17920
- D2= WO-A-03/91189
- D3= The Journal of Pharmacology and Experimental Therapeutics, vol. 301
no. 2, 2002, pages 679-689
- D4= Journal of Medicinal Chemistry, vol. 43, no. 20, 2000, pages 3778-3785
- D5= Journal of Organic Chemistry, vol. 69, no. 15, 2004, pages 5147-5149
- D6= Journal of Organic Chemistry, vol. 69, no. 15, 2004, pages 7700-7704
- D7= Journal of Bioscience and Bioengineering, vol. 92, no. 2 pages 193-196
- D8= Bioorganic & Medicinal Chemistry Letters, vol. 6, no. 2, 1996, pa-
ges 189-194

SECTION III

Claims 34-39 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

For the assessment of the subject-matter of present claims 34-39 on the question whether it is industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claim. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

SECTION V

1. The present application relates to compounds of formula I, processes for their preparation, pharmaceutical compositions comprising them and the use thereof for the manufacture of medicaments.

2. Document D1 discloses a biphenyl derivative of formula 25 (cf. D1, page 19), having the same biological properties (CB₁ binding affinity) and use as the compounds of the present invention (cf. D1, page 1, lines 14-21, page 13, line 18 - page 15, line 18, Table 2, claims 1, 11, 14, 18, 20 and 22). Thus, the disclosure of D1 is prejudicial to the novelty of present claims 1-5, 8, 9, 11, 13-16 and 18-42. The compounds according to D2-D4 also exhibit CB₁ binding affinities (cf. D2, Table 1, entries 1-3; D3, Table 1, entries 1-3; D4, Scheme 2, compounds 20 a,b and Table 5) and are novelty-destroying to present claims 1-5, 8, 9, 11, 13-16 and 18. In D5-D7 a number of compounds are disclosed (cf. D5, Scheme 1, compound 4; D7, Table 2, entry 3; D7, Fig. 1, last reaction scheme) which fall within the scope of present claims 1-5, 8-10, 13-16 and 18.

Accordingly, the subject-matter of claims 1-5, 8, 9, 11, 13-16 and 18-42 does not meet the requirements of Art. 33(2) PCT.

3. The compounds of present claim 1 represent a selection from the compounds of formula I according to D1 which have the same biological properties and use. Such a selection can only be regarded as inventive, if the claimed derivatives possess surprising effects or unexpected advantages in relation to the compounds disclosed in this document. However, no evidence of such effects or properties is presented in the application. Having regard to the fact that the novelty-destroying compounds described in D2-D7 fall within the scope of claim 1 according to D1, the present invention lacks an inventive step in view of D2-D7 when combined with D1. This also applies with respect to 3',5'-dimethyl-4-(1,1-dimethylheptyl)-1,1'-biphenyl-2-ol (cf. D8, Table 4, Scheme 1, compound 14) which has been disclaimed from present claims 1-18.

Thus, the subject-matter of claims 1-5, 8, 9, 11, 13-16 and 18-42 (as far as they are novel) as well as that of claims 6, 7, 10, 12, 17 and 45 does not meet the requirements of Article 33(3) PCT.

4. Process claims 43 and 44 do not appear to contain any features which meet the requirements of the PCT in respect of novelty and/or inventive step.

5. Since the compounds according to D1-D7 are highly relevant for the assessment of inventive step, they cannot be removed from the present claims by means of disclaimers. Moreover, the common concept linking together the compounds of claim 1 is not novel in view of D1. The subject-matter of claim 1 is therefore not so linked as to form a single general inventive concept within the meaning of Rule 13.1 PCT.

In order for claims using a Markush (generic) formula to be regarded as uniform, the claimed compounds should have in common a structural moiety which is distinctive in view of the prior art. This can be achieved by limiting one of the present variables to a single value not occurring in D1.

SECTION VII

Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in documents D1-D4 is not mentioned in the description, nor are these documents identified therein.

SECTION VIII

1. The expression "about" in connection with ranges (cf. page 17, lines 30-32 and page 18, lines 1-2) as well as the phrases "and the like" (cf. page 19, line 21 and page 20, line 5) and "etc." (cf. page 16, line 3 and page 23, line 6) render the scope of the application unclear (Art. 6 PCT).
2. The vague statement in the description on page 59, last paragraph implies that the subject-matter for which protection is sought may be different to that defined by the claims, thereby resulting in lack of clarity (Article 6 PCT) when used to interpret them (see also the PCT Guidelines, PCT/GL/3 III, 4.3a).